

REVIEW

Post-exposure prophylaxis for blood borne viral infections in healthcare workers

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Healthcare workers have a high risk of occupational exposure, more so in developing countries, with high incidence of blood borne diseases and prevalence of unsafe practices. Among the various blood borne diseases, the most common and important ones are HIV infection, hepatitis B, and hepatitis C. Most of the occupational transmission can be prevented and the "standard precaution" has been shown to reduce exposures and hence the transmission of infection. Healthcare workers have to be educated about post-exposure prophylaxis and each institution needs to adopt a clear protocol.

with HIV infected blood and after mucous membrane exposure is 0.3% and 0.09% respectively.^{8,9} Though HIV transmission occurring through intact skin has been documented¹⁰ the risk has not been precisely quantified, but the risk of transmission can be estimated to be far less than that of mucous membrane exposure.¹¹ The risk associated with a single parenteral exposure to blood from a source patient who has HBV infection ranges from 6% in HBV "e" antigen negative patients to as high as 40% in "e" antigen positive.¹² The average incidence of seroconversion to HCV after needlestick injury from an HCV positive source is 1.8% (range 0%–7%).¹³

Healthcare workers in developing countries are at serious risk of infection from blood borne pathogens because of the high prevalence of these pathogens and the increased risk of occupational injuries.^{14,15} Unsafe practices like careless handling of contaminated needles, unnecessary injections on demand, reuse of inadequately sterilised needles, and improper disposal of hazardous waste can increase the potential risk of occupational transmission of these blood borne pathogens.¹⁶

The risk of healthcare workers acquiring a blood borne pathogen after an occupational exposure depends on multiple factors^{17–19}:

(1) Prevalence of infection in the specific population: high prevalence of these pathogens in developing countries substantially increases the risk of occupational exposure.

(2) Frequency of activities capable of transmitting the infectious agent: the increased risk of occupational injuries in the developing countries due to unsafe practices.

(3) Nature and efficacy of transmission of exposure: percutaneous injury has increased risk of transmission compared with exposure to mucous membrane or skin.

(4) Virus present in the contaminated fluid and the viral load: more patients with advanced disease and high viral load in developing countries, as they cannot afford antiretroviral therapy.

(5) Availability and efficacy of pre-exposure and post-exposure prophylaxis: proper guidelines still do not exist in developing countries.

Discussion on post-exposure management would not be complete without at least a mention

Blood borne pathogens acquired through occupational exposure are a major professional hazard among healthcare workers, and the AIDS epidemic has led to intense concern. Over 20 pathogens have been transmitted to healthcare workers via a needlestick injury¹ and the most important are HIV, hepatitis B virus (HBV) and hepatitis C virus (HCV) (see box 1). According to estimates from the joint United Nations Programme on HIV/AIDS and the World Health Organisation, 40 million adults and 2.7 million children were living with HIV at the end of 2001² and there are about 400 million people worldwide who are chronic carriers of HBV. Among healthcare workers seroprevalence of HBV is two to four times higher than that of general population.³ Physicians, dentists, laboratory workers, dialysis workers, cleaning service employees, and nurses have highest prevalence.^{3,4} More than 90% of the infected persons in general population live in the developing world. The available data from developing countries show that adherence to the "standard precaution" and adequate documentation of occupational exposures are suboptimal and the knowledge about post-exposure prophylaxis among healthcare workers is poor.^{5,6} In developing countries where even the basic medical care is inadequate, protecting the healthcare worker is a formidable challenge.

RISK OF OCCUPATIONAL TRANSMISSION OF INFECTION

Since the first report in 1984 of a healthcare worker developing HIV infection after a needlestick injury⁷ there has been a great concern about the occupational transmission of blood borne pathogens. The estimated risk for HIV transmission after injury through a needle contaminated

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Abbreviations: HBV, hepatitis B virus; HCV, hepatitis C virus; NNRTI, non-nucleoside reverse transcriptase inhibitors; NRTI, nucleoside analogue reverse transcriptase inhibitors

Box 1: Diseases transmitted by needlestick to healthcare workers

- Blastomycosis.
- Brucellosis.
- Cryptococcosis.
- Diphtheria.
- Ebola virus.
- Hepatitis B.
- Hepatitis C.
- Herpes simplex.
- HIV.
- Leptospirosis.
- Malaria.
- *Mycobacterium marinum*.
- *Mycoplasma caviae*.
- Rocky Mountain spotted fever.
- Syphilis.
- Toxoplasmosis.
- Tuberculosis.
- Varicella zoster.

of primary prevention strategies. Therefore, implementing behaviour modification in the workplace designed to reduce the risks for occupational exposure to blood borne pathogens remains the cornerstone of all prevention strategies.

Healthcare workers should be:

- (1) Made aware of the risks existing in the workplace.
- (2) Educated about the magnitude of such risks.
- (3) Trained in reducing exposure risk minimising strategies ("standard precautions" previously called universal precautions) such as:
 - All patients to be treated as potential carriers of blood borne pathogens.
 - Use of appropriate personal protective equipments like glove, mask, gown, eye protection wares, etc during procedures where contamination of blood or body fluids are likely.
 - Careful handling of sharps and avoiding sharp injury.
 - Proper disposal of sharps and infectious waste.
- (4) Provided training to modify procedures that have high risk; and
- (5) Provided with instruments and devices that reduce exposure risks through advanced manufacturing technology.²⁰

An important aspect of managing blood borne pathogens in the healthcare setting is the development of an institutional policy for post-exposure management of healthcare workers who are occupationally exposed to these pathogens.

DEFINITION OF EXPOSURE

"Exposure" to blood, tissue, or other body fluids like semen, vaginal secretions, cerebrospinal, pleural, peritoneal, pericardial, synovial, and amniotic fluids have a potential risk of transmission of blood borne pathogens to healthcare workers and therefore post-exposure prophylaxis should be considered if there is²¹:

- (1) A percutaneous injury (for example, a needlestick or cut with a sharp object).
- (2) Contact with mucous membrane or non-intact skin (for example, skin chapped or abraded or dermatitis).
- (3) Prolonged contact with intact skin or contact that involves extensive areas of skin.

FACTORS INFLUENCING RISK OF TRANSMISSION

Factors influencing risk of transmission are:

- (1) Depth of the injury (in case of a sharp object).
- (2) Device was visibly contaminated with blood.

- (3) Needle that was directly inside an artery or vein.
- (4) Type of needle: a hollow bore or a solid needle.
- (5) The thickness of the needle.
- (6) Viral load of the source.
- (7) Quantity of blood or body fluid exposed.
- (8) Duration of exposure.

GENERAL MEASURES TO BE TAKEN AFTER AN EXPOSURE

The following general guidelines are recommended as soon as potential exposure to blood or contaminated body fluids occurs.

Treatment to the exposed site

Wounds and skin sites that have been in contact with blood or body fluids should be washed with soap and water; mucous membranes like eye or mouth should be flushed with water. The use of antiseptics is encouraged. However there is no evidence that the use of antiseptics for wound care or expressing fluid by further squeezing the wound reduces the risk for HIV transmission. The application of caustic agents or instillation of antiseptics or disinfectants into the wound is not recommended.

Documentation of the data

Trained medical personnel should document the data in the medical record:

- Name and data of the source.
- Time and date of exposure.
- Nature of exposure (that is, non-intact skin, mucosal, or percutaneous exposure).
- Body site exposed and contact time.
- Infective status of the source if documented.
- For percutaneous injuries, a description of the injury (depth of wound, solid versus hollow needle, sharp, etc).
- Circumstances under which the exposure incident occurred.
- Previous testing and immune status of the exposed healthcare worker.

Testing of source

Testing of the source for HIV, HBsAg, and HCV should be done as early as possible after counselling (rapid testing if available) if infective status is not known already.

POST-EXPOSURE PROPHYLAXIS OF HIV INFECTION**Rationale of post-exposure prophylaxis**

The rationale for post-exposure prophylaxis is based on the following factors:

- (1) Pathogenesis of HIV infection.
- (2) The biological plausibility that using antiretroviral drugs can prevent transmission.
- (3) The risk benefits of post-exposure prophylaxis to exposed healthcare workers.

The knowledge about primary HIV infection indicates that systemic infection does not occur immediately, leaving a brief "window of opportunity" during which post-exposure antiretroviral intervention may modify viral entry into cell and replication. Data from animal studies have been difficult to interpret because a lack of a comparable animal model and the need to have a higher inoculum than that expected after exposure to needlestick injuries.²¹ However animal studies have demonstrated that early initiation of post-exposure prophylaxis and small inoculum size correlates with successful post-exposure prophylaxis.

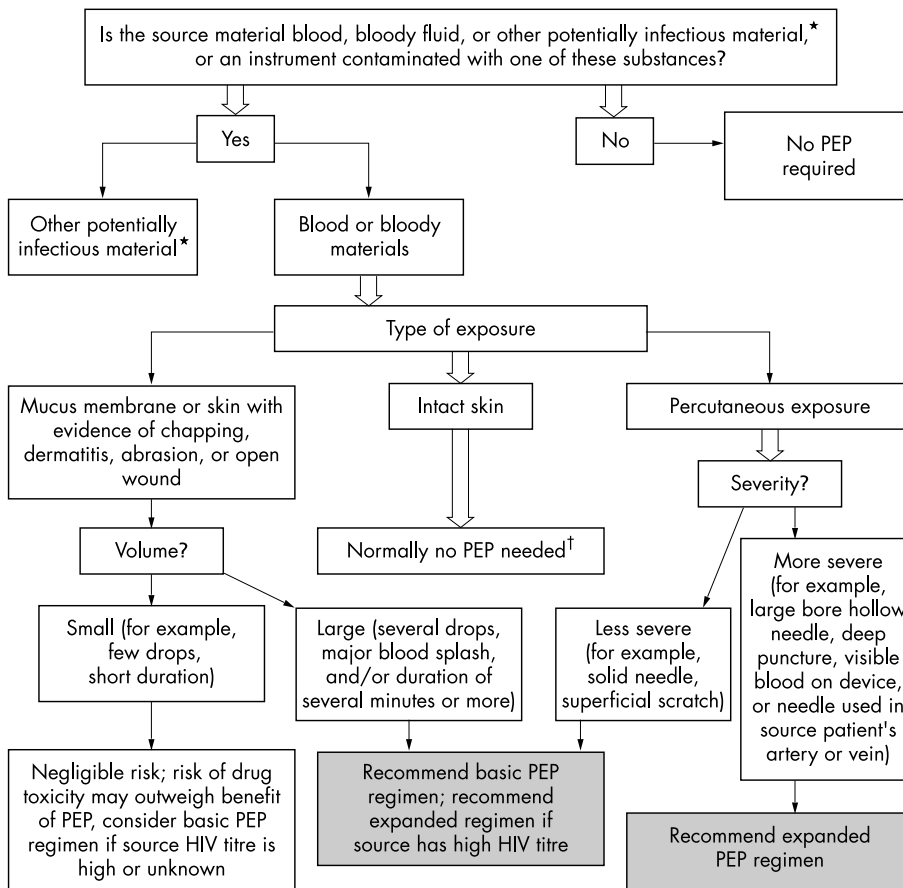


Figure 1 Centers for Disease Control and Prevention guidelines for evaluating the risk of HIV transmission after occupational exposure (PEP, post-exposure prophylaxis). *Other potentially infectious materials include semen; vaginal secretions; cerebrospinal, synovial, pleural, peritoneal, pericardial, or amniotic fluids; or tissue. These body substances generally carry a low risk of infection in healthcare settings. Unprotected contact with concentrated HIV requires clinical evaluation to determine the need for post-exposure prophylaxis. †Consider post-exposure prophylaxis if extensive area was exposed or if prolonged contact with blood occurred.

No randomised clinical trials have evaluated the efficacy of post-exposure prophylaxis in humans. In a retrospective case control study among healthcare workers, the risk for HIV infection in those who used zidovudine as post-exposure prophylaxis reduced by 81%.²² Antiretroviral therapy has also been demonstrated to reduce maternal-infant transmission of HIV.²³ Failure of zidovudine also has been reported in few instances.²¹

The risk of transmission can be assessed using the flow chart shown in fig 1.

Selection of post-exposure prophylaxis regimen

Selection of the post-exposure prophylaxis regimen should be decided after considering comparative risk represented by the exposure and information about the source patient including details of antiretroviral therapy and current clinical condition based upon CD4 counts, viral load, and stage of the disease. Among the several antiretroviral agents available from at least three classes of drugs—nucleoside analogue reverse transcriptase inhibitors (NRTI), non-nucleoside reverse transcriptase inhibitors (NNRTI), and protease inhibitors—zidovudine has been proved to prevent transmission of HIV in humans.^{22–24} Hence based on the available data, zidovudine has been recommended as the first drug of choice in all post-exposure prophylaxis regimens.

There are no data to directly support the addition of other antiretroviral drugs to zidovudine to enhance the effectiveness of the post-exposure prophylaxis regimen. However in HIV infected patients combination regimens have proved superior to monotherapy in reducing viral load.^{25–26} Thus, theoretically a combination of drugs with activity at different stages in the viral replication cycle (for example, NRTI with a protease inhibitor) could offer an additive preventive effect in post-exposure prophylaxis, particularly for occupational expo-

sure that pose an increased risk for transmission. Determining which and how many such agents are needed is largely empiric.

Lamivudine is recommended as the second agent for post-exposure prophylaxis based on the greater antiretroviral activity of a zidovudine/lamivudine combination as well as its activity against many zidovudine resistant HIV strains without substantial increase in toxicity.²⁷ Most HIV exposures will warrant only a two drug regimen using two NRTIs, usually zidovudine and lamivudine. The other two NRTIs commonly used are a combination of lamivudine and stavudine. The addition of a third drug, usually a protease inhibitor (that is, indinavir or nelfinavir), or efavirenz, an NNRTI, should be considered for exposures that pose an increased risk for transmission or where resistance to the other drugs for post-exposure prophylaxis is known or suspected. Indinavir has been preferred as the third drug when needed because of its increased bioavailability and better toxicity profile during short term use. Although side effects might be common with the NNRTIs, efavirenz might be considered for expanded post-exposure prophylaxis regimens,²⁸ especially due to lower cost of therapy. Nevirapine and delavirdine have not been routinely recommended because of their increased risk of hepatotoxicity.

Currently, two types of regimen are recommended for post-exposure prophylaxis—a “basic” two drug regimen and an “expanded” three drug regimen that should be used for exposures that pose an increased risk for transmission (table 1).

Timing for post-exposure prophylaxis and monitoring for toxicity

Post-exposure prophylaxis should be initiated as soon as possible (that is, within a few hours). Although animal studies suggest that it is probably substantially less effective when started more than 24–36 hours post-exposure, the interval

Table 1 Basic and expanded regimens for post-exposure prophylaxis for HIV

Type	Drugs
Basic (28 days)	Zidovudine 300 mg twice a day + lamivudine 150 mg twice a day or Stavudine 30–40 mg twice a day + lamivudine 150 mg twice a day
Expanded (28 days)	Indinavir 800 mg three times a day or Nelfinavir 750 mg three times a day or Efavirenz 600 mg once a day

Table 2 Common side effects of drugs given for post-exposure prophylaxis for HIV

Drug	Dose	Common side effects/comments
NRTIS		
Zidovudine	300 mg twice a day	Initial nausea, anaemia, neutropenia, myopathy
Lamivudine	150 mg twice a day	Generally well tolerated
Stavudine	40 mg twice a day for >60 kg body weight 30 mg twice a day for <60 kg body weight	Peripheral neuropathy Should not be coadministered with zidovudine
Protease inhibitors		
Indinavir sulphate	800 mg three times a day on empty stomach or with snack containing <2 g of fat	Kidney stones, occasional nausea, abdominal pain, and gastrointestinal upset. Store in original container which contains desiccant; without this, indinavir is stable for only about three days
NNRTI		
Efavirenz	600 mg once daily	Rash (including Stevens-Johnson syndrome), insomnia, dizziness, and abnormal dreaming

after which no benefit is gained from post-exposure prophylaxis for humans is undefined. Therefore, if appropriate for the exposure, it should be started even when the interval since exposure exceeds 36 hours. Initiating therapy after a longer interval (for example, one week) might be considered for exposures that represent an increased risk for transmission. The optimal duration of post-exposure prophylaxis is unknown but four weeks is the generally accepted course. Drug toxicity monitoring should be performed at baseline and again two weeks after starting post-exposure prophylaxis. The common side effects are listed in table 2. Testing should include total and differential blood count, renal function tests (for patients receiving indinavir), and liver function tests. Blood glucose should be monitored if a protease inhibitor is included in the regimen. If indinavir is used monitoring for crystalluria, haematuria, and hepatitis should be done. If toxicity is noted modification of the regimen should be considered.

Antiretroviral drugs during pregnancy

Data are limited on the potential effects of antiretroviral drugs on the developing fetus or neonate. The decision to use any antiretroviral drug during pregnancy should involve discussion between the woman and her healthcare provider regarding the potential benefits and risks to her and her fetus. Certain drugs should be avoided in pregnant women. Because teratogenic effects were observed in primate studies, efavirenz is not recommended during pregnancy. Reports of fatal lactic acidosis in pregnant women treated with a combination of stavudine and didanosine have prompted warnings about these drugs during pregnancy. Because of the risk of hyperbilirubinaemia in newborns, indinavir should not be administered to pregnant women shortly before delivery.

Evaluation of healthcare workers for seroconversion and need for post-exposure prophylaxis

If the source individual is HIV positive, the exposed worker should be evaluated for HIV seroconversion with baseline HIV testing and follow up testing at six weeks, three months, and

six months.²⁹ In 95% of cases, seroconversion occurs within six months after the exposure.²¹ The need for post-exposure prophylaxis should be decided depending on the seriousness of exposure (for example, severe: large bore hollow needle with visible blood or the one used in source patient's artery or vein that has caused deep puncture in the exposed person; mild: few drops of blood splashed on to the skin or mucus membrane for a transient period) and stage of HIV disease of the source patient.

POST-EXPOSURE PROPHYLAXIS FOR HEPATITIS B INFECTION

For percutaneous or mucosal exposures to blood, several factors must be considered when making a decision to provide prophylaxis, including the HBsAg status of the source and the hepatitis B vaccination and vaccine response status of the exposed person. Consistent and appropriate use of the HBV vaccine is the cornerstone of all prevention and control strategies related to the occupational risks associated with HBV in the healthcare workplace. The vaccine is safe and effective, producing immunity in more than 90% of those immunised.^{30–31} Currently, HBV vaccination is mandatory for healthcare workers who are involved in patient care directly or those who handle blood or blood products.

Post-exposure prophylaxis for HBV infection should be given to those who are exposed percutaneously or through mucus membrane to blood or body fluids of known or suspected

HBsAg positive individual: If the source individual is HBsAg positive and the exposed person is unvaccinated or antibody level is less than 10 mIU/ml, hepatitis B immunoglobulin (0.6 ml/kg) should be administered (preferably within 24 hours) along with the vaccine series given at a different site.²⁹ The chance of seroconversion can be reduced by 90% with this post-exposure prophylaxis.³² The effectiveness of HBIG when administered >7 days after exposure is unknown. If the exposed healthcare worker was vaccinated earlier and had an

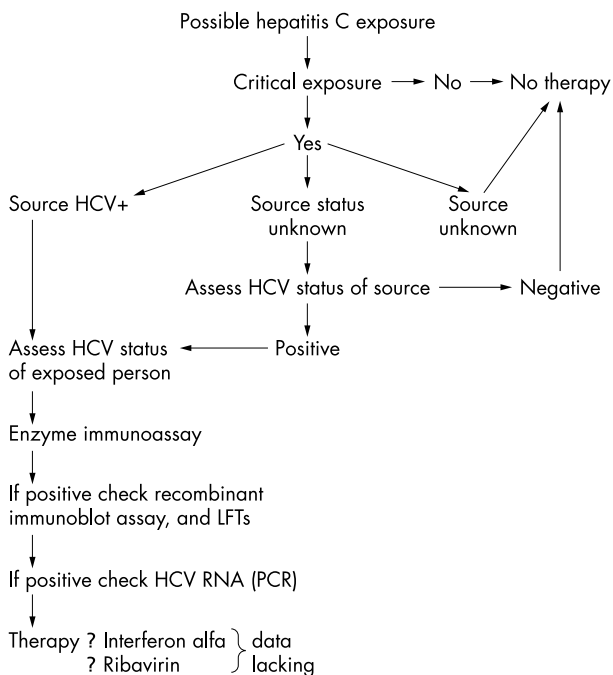


Figure 2 Management of exposure to hepatitis C virus (LFTs, liver function tests; PCR, polymerase chain reaction).

adequate antibody response (>10 mIU/ml) no treatment is required. If the source patient's status is unknown and the exposed person was not vaccinated or antibody response was inadequate, initiate the vaccine series.

MANAGEMENT OF EXPOSURE TO HEPATITIS C INFECTION (SEE FIG 2)

At present, there is no proved effective post-exposure prophylaxis for healthcare workers exposed to HCV. Immunoglobulin and antiviral agents are not recommended for post-exposure prophylaxis of HCV. Limited data indicate the antiviral therapy using interferon and ribavirin might be beneficial when started early, but no guidelines exists for administration of therapy during the acute phase of infection.¹¹

The following are recommendations for follow up of occupational HCV exposures:

- For the source perform testing for anti-HCV.
- For the person exposed to an HCV positive source perform baseline testing for anti-HCV and alanine aminotransferase activity and follow up testing (for example, at 4–6 months) for anti-HCV and alanine aminotransferase activity (if earlier diagnosis of HCV infection is desired, testing for HCV RNA may be performed at 4–6 weeks).

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